

Applicant : Vincent P. Stan
Serial No. :
Filed : HEREWITH
Page : 15

Attorney's Docket No.: 11926-015002

REMARKS

The amendment to the specification is made solely to insert the Sequence Listing and SEQ ID NOS. into the specification. No new matter is introduced. The accompanying declaration by the inventor confirms that the sequences in the Sequence Listing are the same as those incorporated by reference into the original specification by providing the GenBank® Accession Number for each sequence. A signed declaration will be filed under separate cover.

Applicant requests that claims 17-49 be examined together without restriction. Each of SEQ ID NOS:6, 7, and 8 relate to the human thymidylate synthetase gene. SEQ ID NO:6 corresponds to the coding region. SEQ ID NO:7 corresponds to the promoter region. SEQ ID NO:9 corresponds to the exons. Three SEQ ID NOS are required even though only one gene is referenced because the original specification identified the sequences by providing three GenBank® Accession Numbers.

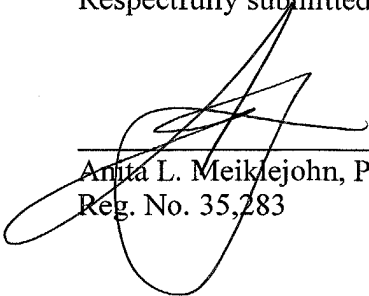
Each of the nucleotides specified in the claims represents a single nucleotide polymorphism in the human thymidylate synthetase gene.

Attached is a marked-up version of the changes being made by the current amendment.

Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 24 Sept 2001



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Applicant : Vincent P. Stanton
Serial No. :
Filed : HEREWITH
Page : 16

Attorney's Docket No.: 11926-015002

Version with markings to show changes made

In the specification:

The paragraph beginning at page 1, line 8, has been amended as follows:

This application is a divisional of U.S. Application Serial No. 09/658,659, filed September 8, 2000, which is a CIP of Stanton, U.S. Application serial No. 09/596,033, filed June 15, 2000 entitled GENE SEQUENCE VARIACNES IN GENES RELATED TO FOLATE METABOLISM HAVING UTILITY IN DETERMINING THE TREATMENT OF DISEASE which is a CIP of Stanton, U.S. Application 09/357,743, filed July 20, 1999, entitled GENE SEQUENCE VARIACNES IN GENES RELATED TO FOLATE METABOLISM HAVING UTILITY IN DETERMINING THE TREATMENT OF DISEASE which is a CIP of Stanton, U.S. Application Serial No. 09/357,024, filed July 19, 1999, entitled GENE SEQUENCE VARIACNES IN GENES RELATED TO FOLATE METABOLISM HAVING UTILITY IN DETERMINING THE TREATMENT OF DISEASE, which claims the benefit of Stanton, U.S. Provisional Application 60/093,484, filed July 20, 1998, entitled GENE SEQUENCE VARIACNES IN GENES RELATED TO FOLATE METABOLISM HAVING UTILITY IN DETERMINING THE TREATMENT OF DISEASE, which are all hereby incorporated by reference in their entireties including drawings and tables.

Table 10 beginning at page 171 has been amended as follows:

Table 10

Variance Table

Hugo	GID	OMIM ID	VGX Symbol	Description
Variance Start	Variance			
U73338	U73338	156570	GEN-69	Methionine
Synthase (SEQ ID NO:1)				
	194	(-201)C>G		5'
	284	(-111)C>T		5'
	1136	742G>A	V248M	
	1252	858C>T	Silent	

Attorney's Docket No.: 11926-015002

D78586	D78586	114010	GEN-BR	CAD PROTEIN (SEQ
ID NO:2)				

U09178 U09178 274270 GEN-HA
Dihydropyrimidine Dehydrogenase (SEQ ID NO:3)

U19720	U19720	600424	GEN-II1	Folate
Transporter	(SLC19A1)	(SEQ ID NO:4)		

175	80G>A	R27H
341	246C>G	Silent
791	696C>T	Silent
1067	972G>A	Silent
1337	1242C>A	Silent
1997	1902T>C	3'
2100	2005^2006insG	3'
2582	2487T>G	3'

Applicant : Vincent P. Stan
Serial No. :
Filed : HEREWITH
Page : 18

Attorney's Docket No.: 11926-015002

2617 2522C>T 3'
2652 2557T>C 3'
U92868 U92868 600424 GEN-LUK Homo sapiens reduced
folate carrier (RFC1) gene, exons 1a, 1c and 1b (SEQ ID NO:5)
431 431A>G Intron
441 441A>G Intron
498 498C>T Intron
579 579G>C Intron
599 599G>C Intron
X02308 X02308 188350 GEN-KL Thymidylate
synthetase (SEQ ID NO:6)
1066 961T>C 3'
1136 1031A>G 3'
1497 1392T>A 3'
D00517 D00517 188350 GEN-LUC Thymidylate
synthase, promoter (SEQ ID NO:7)
276 276C>T Intron
321 321T>C Intron
452 452G>A Intron
457 457^insC Intron
491 491C>A Intron
533 533T>C Intron
624 624A>C Intron
639 639A>G Intron
655 655T>C Intron
D00596 D00596 188350 GEN-LUD Homo sapiens
gene for thymidylate synthase, exons 1, 2, 3, 4, 5, 6, 7,
complete cds (SEQ ID NO:8)
701 701A>C Intron
716 716A>G Intron
732 732T>C Intron
1293 1293A>G Intron
1322 1322C>G Intron
1379 1379T>C Intron
1590 1590C>T Intron
1688 1688C>G Intron
2401 2401A>G Intron
2429 2429G>A Intron
2488 2488C>T Intron
2594 2594G>T Intron
2618 2618G>A Intron
3083 3083G>A Intron
3125 3125G>A Intron
3212 3212C>T Intron
3619 3619T>A Intron

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Applicant : Vincent P. Starck Jr.
Serial No. :
Filed : HEREWITH
Page : 19

Attorney's Docket No.: 11926-015002

3635	3635G>A	Intron
4256	4256G>A	Intron
4898	4898A>G	Intron
5006	5006C>T	Intron
5062	5062G>A	Intron
5167	5167G>A	Intron
11069	11069A>G	Intron
11238	11238C>T	Intron
11293	11293T>G	Intron
11422	11422T>C	Intron
11686	11686C>T	Intron
12598	12598T>C	Intron
13171	13171T>C	Intron
13298	13298G>A	Intron
13645	13645T>C	Intron
13751	13751C>A	Intron
13782	13782T>C	Intron
13806	13806T>C	Intron
13813	13813T>C	Intron
14479	14479A>G	Intron
14546	14546^insT	Intron
14585	14585C>T	Intron
14729	14729G>A	Intron
14787	14787C>T	Intron
14795	14795G>A	Intron
15041	15041T>C	Intron
15343	15343G>A	Intron
15449	15449G>A	Intron
15502	15502G>A	Intron
15545	15545C>T	Intron
15589	15589A>G	Intron
15769	15769C>T	3'
15839	15839A>G	3'
16148	16148G>A	3'
16198	16198T>G	3'
16202	16202G>T	Intron

X59618	X59618	180390	GEN-M3	Ribonucleotide
reductase M2	polypeptide	(SEQ ID NO:9)		
128		(-67)G>A		5'
189		(-6)T>G		5'
524		330C>G	Silent	
1399		1205T>A		3'
1464		1270G>A		3'
1636		1442C>T		3'
1738		1544C>T		3'

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Attorney's Docket No.: 11926-015002

	2259	2065T>C	3'
S72487	S72487	131222	GEN-3LD
phosphorylase, partial	<u>(SEQ ID NO:10)</u>		Thymidine
	183	19G>A	D7N
	483	319C>T	3'
	601	437G>C	3'
	1299	1135G>A	3'

M58602 M58602 131222 GEN-LUB Thymidine
phosphorylase, promoter and genomic (SEQ ID NO:11)

124	124C>T	3'
439	439G>A	3'
1044	1044^insCT	3'
1331	1331G>A	3'
1977	1977G>A	Intron
2149	2149G>A	Intron
2467	2467A>G	Intron
2634	2634C>G	Intron
2975	2975G>A	Intron
3116	3116G>T	Intron
3255	3255A>C	Intron
3344	3344T>C	Intron
4051	4051C>A	Intron
4782	4782G>A	Intron
5022	5022T>C	Intron
5266	5266G>A	Intron
5285	5285C>G	Intron
5438	5438T>A	Intron
5482	5482C>T	Intron
5629	5629G>A	Intron
5648	5648C>T	Intron
5731	5731G>A	Intron

M98045 M98045 136510 GEN-4C3 Homo sapiens
folylpolyglutamate synthetase mRNA, complete cds (SEQ ID NO:12)

802	732C>T	Silent
1747	1677G>T	3'
1900	1830T>C	3'

U24253 U24253 136510 GEN-LUE Human
folylpolyglutamate synthetase (FPGS) gene, exons 5-11, and
partial cds (SEQ ID NO:13)

1424	1424C>A	Intron
1649	1649G>A	Intron
2554	2554A>G	Intron

U24252 U24252 136510 GEN-LUF
Folylpolyglutamate synthetase, promoter and exons 1-4 (SEQ ID
NO:14)

1. 1990年12月31日	
流动资产	1,000,000
长期资产	2,000,000
负债	1,500,000
所有者权益	1,500,000
总资产	3,000,000
总负债及所有者权益	3,000,000
2. 1991年12月31日	
流动资产	1,200,000
长期资产	2,200,000
负债	1,600,000
所有者权益	1,600,000
总资产	3,400,000
总负债及所有者权益	3,400,000
3. 1992年12月31日	
流动资产	1,400,000
长期资产	2,400,000
负债	1,700,000
所有者权益	1,700,000
总资产	3,800,000
总负债及所有者权益	3,800,000
4. 1993年12月31日	
流动资产	1,600,000
长期资产	2,600,000
负债	1,800,000
所有者权益	1,800,000
总资产	4,200,000
总负债及所有者权益	4,200,000
5. 1994年12月31日	
流动资产	1,800,000
长期资产	2,800,000
负债	1,900,000
所有者权益	1,900,000
总资产	4,600,000
总负债及所有者权益	4,600,000
6. 1995年12月31日	
流动资产	2,000,000
长期资产	3,000,000
负债	2,000,000
所有者权益	2,000,000
总资产	5,000,000
总负债及所有者权益	5,000,000
7. 1996年12月31日	
流动资产	2,200,000
长期资产	3,200,000
负债	2,100,000
所有者权益	2,100,000
总资产	5,400,000
总负债及所有者权益	5,400,000
8. 1997年12月31日	
流动资产	2,400,000
长期资产	3,400,000
负债	2,200,000
所有者权益	2,200,000
总资产	5,800,000
总负债及所有者权益	5,800,000
9. 1998年12月31日	
流动资产	2,600,000
长期资产	3,600,000
负债	2,300,000
所有者权益	2,300,000
总资产	6,200,000
总负债及所有者权益	6,200,000
10. 1999年12月31日	
流动资产	2,800,000
长期资产	3,800,000
负债	2,400,000
所有者权益	2,400,000
总资产	6,600,000
总负债及所有者权益	6,600,000
11. 2000年12月31日	
流动资产	3,000,000
长期资产	4,000,000
负债	2,500,000
所有者权益	2,500,000
总资产	7,000,000
总负债及所有者权益	7,000,000
12. 2001年12月31日	
流动资产	3,200,000
长期资产	4,200,000
负债	2,600,000
所有者权益	2,600,000
总资产	7,400,000
总负债及所有者权益	7,400,000
13. 2002年12月31日	
流动资产	3,400,000
长期资产	4,400,000
负债	2,700,000
所有者权益	2,700,000
总资产	7,800,000
总负债及所有者权益	7,800,000
14. 2003年12月31日	
流动资产	3,600,000
长期资产	4,600,000
负债	2,800,000
所有者权益	2,800,000
总资产	8,200,000
总负债及所有者权益	8,200,000
15. 2004年12月31日	
流动资产	3,800,000
长期资产	4,800,000
负债	2,900,000
所有者权益	2,900,000
总资产	8,600,000
总负债及所有者权益	8,600,000
16. 2005年12月31日	
流动资产	4,000,000
长期资产	5,000,000
负债	3,000,000
所有者权益	3,000,000
总资产	9,000,000
总负债及所有者权益	9,000,000
17. 2006年12月31日	
流动资产	4,200,000
长期资产	5,200,000
负债	3,100,000
所有者权益	3,100,000
总资产	9,400,000
总负债及所有者权益	9,400,000
18. 2007年12月31日	
流动资产	4,400,000
长期资产	5,400,000
负债	3,200,000
所有者权益	3,200,000
总资产	9,800,000
总负债及所有者权益	9,800,000
19. 2008年12月31日	
流动资产	4,600,000
长期资产	5,600,000
负债	3,300,000
所有者权益	3,300,000
总资产	10,200,000
总负债及所有者权益	10,200,000
20. 2009年12月31日	
流动资产	4,800,000
长期资产	5,800,000
负债	3,400,000

Attorney's Docket No.: 11926-015002

Serial No. :
Filed : HERewith
Page : 21

Attorney's Docket No.: 11926-015002

263	263A>G	Intron
266	266G>T	Intron
527	527C>G	Intron
1037	1037A>G	5'
1139	1139G>A	Intron
1217	1217C>T	Intron
1647	1647C>T	Intron
1955	1955G>A	Intron
2017	2017G>A	Intron
2037	2037G>A	Intron
2189	2189A>G	Intron
2282	2282C>T	Intron
2309	2309A>G	Intron

U09806 U09806 236250 GEN-4FZ Human
methylenetetrahydrofolate reductase mRNA, partial cds (SEQ ID
NO:15)

120	120T>C	Silent
464	464T>G	M155R
519	519C>T	Silent
668	668C>T	A223V
1059	1059T>C	Silent
1289	1289C>A	3'
1308	1308T>C	3'
1784	1784G>A	3'

AF061655 AF061655 123920 GEN-LUJ Cytidine
deaminase, promoter (SEQ ID NO:16)

575	575T>C	Intron
648	648T>C	Intron
771	771G>C	Intron
883	883G>A	Intron
941	941^insC	5'
1051	1051A>C	K27Q

1990年12月31日	
资产	负债及所有者权益
流动资产	流动负债
货币资金	短期借款
应收账款	应付账款
预付账款	预收账款
其他应收款	其他应付款
存货	应付工资
流动资产合计	流动负债合计
长期资产	长期负债
固定资产	长期借款
无形资产	应付债券
长期股权投资	长期应付款
长期资产合计	长期负债合计
所有者权益	
实收资本	
资本公积	
盈余公积	
未分配利润	
所有者权益合计	
资产总计	负债及所有者权益总计